

Preparation and Reactions of 2,5-Dimethoxythiophen

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2,5-Dimethoxythiophen, prepared from 2,5-di-iodothiophen, undergoes some electrophilic substitution reactions but is susceptible to ring opening by mineral acid. It is also decomposed by butyl-lithium. Reaction with maleic anhydride in xylene proceeds with extrusion of sulphur and a second Diels–Alder reaction to give a bis-adduct (2).

THE only dimethoxythiophen which has been fully described is the 3,4-isomer.¹ Although the 2,5-isomer has been mentioned,² no reactions or method of preparation were described. We have prepared 2,5-dimethoxythiophen by an extension of the method of Sicé³ for 2-methoxythiophen. Its reactions, summarised in the Scheme, showed both expected and unexpected features. Electrophilic substitution was successful only in the cases shown; Friedel–Crafts acylation with a variety of catalysts, bromination with pyridinium hydrobromide perbromide, and nitration with copper(II) nitrate in acetic anhydride failed.

The failure of these reactions indicated that the molecule might be susceptible to acid. Indeed 2,5-dimethoxythiophen was converted by dilute hydrochloric acid into methyl 2-methoxythiocarbonylpropionate (1). This is apparently the first example of ring opening of a thiophen under such mild conditions, and indicates that 2,5-dimethoxythiophen has limited aromatic stability; we therefore investigated its behaviour towards a dienophile.

Reaction with maleic anhydride in refluxing xylene afforded a crystalline product which was not the expected 3,6-dimethoxyphthalic anhydride (which might have arisen by loss of hydrogen sulphide⁷ from the initial

1:1 Diels–Alder adduct). Spectroscopic and other evidence (see Experimental section) showed that the compound had structure (2); a suggested mechanism for its formation is given in the Scheme. No Diels–Alder reaction between a simple thiophen and maleic anhydride has been recorded. However, Helder and Wynberg⁸ obtained phthalonitriles from but-2-ynedinitrile (an extremely reactive dienophile) and certain thiophens; this reaction also involved extrusion of sulphur.

EXPERIMENTAL

Details of experiments shown in the Scheme but not described here are available as Supplementary Publication No. SUP 21476 (5 pp.).†

2,5-Dimethoxythiophen.—Freshly dried copper(II) oxide (65 g) and 2,5-di-iodothiophen (171 g) were added to a solution of sodium methoxide [from sodium (133 g)] in absolute methanol (1 l). The mixture was boiled under reflux with stirring for 32 h, then cooled and filtered. The solids were washed with methanol, the washings were combined with the main filtrate, and the methanol was removed under reduced pressure. Water was added to the residue; the crude product was isolated with ether and was distilled to yield 2,5-dimethoxythiophen (19.5 g, 27%) as a pale yellow oil, b.p. 94–96° at 20 mmHg (Found: S, 22.2.

¹ E. W. Fager, *J. Amer. Chem. Soc.*, 1945, **67**, 2217; G. C. Overberger and J. Lal, *ibid.*, 1951, **73**, 2956.

² A. Tundo, *Boll. sci. Fac. Chim. ind. Bologna*, 1960, **18**, 102.

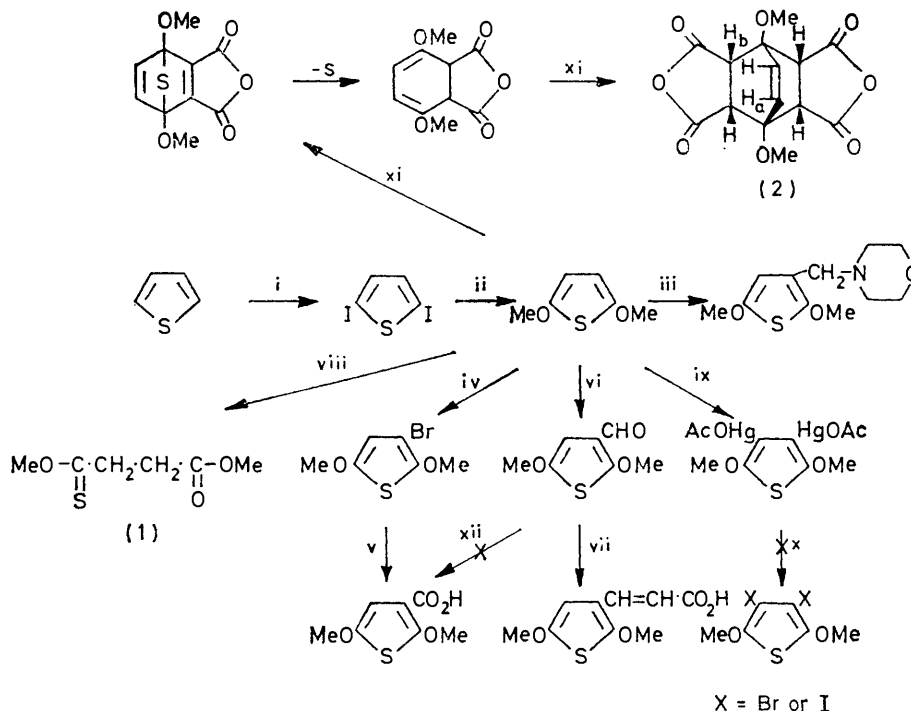
³ J. Sicé, *J. Amer. Chem. Soc.*, 1953, **75**, 3697.

† For details of Supplementary Publications see Notice to Authors No. 7, *J.C.S. Perkin I*, 1974, Index issue.

Calc. for $C_6H_8O_2S$: S, 22.2%, τ (CCl_4) 6.40 (s, CH_3O) and 4.48 (s, ArH), ν_{max} (film) 2 910 and 2 805 (both m) and 1 455s and 1 240s cm^{-1} .

Reaction of 2,5-Dimethoxythiophen with Acid.—A solution of 2,5-dimethoxythiophen (3 g) in ether (10 ml) was stirred overnight with aqueous hydrochloric acid (5 ml concentrated acid + 10 ml water) in such a way that constant mixing of the layers occurred. T.l.c. (SiO_2 ; benzene) then showed that all the dimethoxythiophen had been consumed. The ethereal solution was washed with water (2 \times), dried

—Maleic anhydride (0.5 g, 5.2 mmol) and the dimethoxythiophen (0.72 g, 5 mmol) were dissolved in dry xylene (8 ml) and the yellow solution was boiled under reflux for 3.5 h (H_2S evolved). The solution was cooled in ice and the solid (0.43 g) was filtered off and recrystallised from acetone-light petroleum (b.p. 60—80°) to give 1,4-dimethoxybicyclo-[2.2.2]oct-7-ene-2,3,5,6-tetracarboxylic dianhydride (2) (0.33 g, 42%) as pale yellow crystals, m.p. 263—264° (Found: C, 54.4; H, 3.9. $C_{14}H_{12}O_8$ requires C, 54.5; H, 3.9%), τ [$(CD_3)_2SO$] 3.79 (2 H, H_a), 5.93 (4 H, H_b), and 6.42 (6 H,



SCHEME Reagents: i, I_2-HNO_3 [cf. ref. 4 (85%); m.p. 41—43°]; ii, NaOMe-MeOH-CuO (cf. ref. 3); iii, CH_2O -morpholine [cf. ref. 4 (53%); b.p. (bath) 150° at 0.5 mmHg]; iv, NBS- CCl_4 [(50%); b.p. 118—126° at 12 mmHg]; v, Bu^oLi-CO_2 [(45%); m.p. 138—139°; direct lithiation with Bu^oLi at room temperature gave a strongly exothermic reaction leading to polymeric products]; vi, $Me_2N-CHO-POCl_3-CH_2Cl_2$ [(39%); m.p. 41—43°]; vii, $CH_2(CO_2H)_2$ -pyridine-piperidine [(27%); m.p. 170—172°]; viii, aq. HCl-Et $_2O$; ix, $Hg(OAc)_2-EtOH$ [(100%); m.p. 217—218° (decomp.)]; x, KI- I_2 or Br_2-CCl_4 (cf. ref. 5); xi, maleic anhydride-xylene; xii, Tollens' reagent (cf. ref. 6)

($MgSO_4$), and evaporated to yield a mobile yellow liquid (2.49 g). Chromatography on silica (25 g; column 8 \times $\frac{3}{4}$ in) provided a fraction (2.03 g), eluted by 1:1 benzene-light petroleum (b.p. 40—60°), that was shown by t.l.c. (SiO_2 ; benzene) to be essentially pure. Distillation gave methyl 2-methoxythiocarbonylpropionate as a liquid, b.p. 120—121° at 16 mmHg (Found: C, 44.25; H, 6.2; S, 20.1. $C_6H_{10}O_3S$ requires C, 44.4; H, 6.2; S, 19.7%), M (v.p. osmometry) 152 (required 162), τ (CCl_4) 7.24 (A_2B_2 , CH_2-CH_2), 6.43 (s, $CS-OCH_3$), and 6.03 (s, $CO-OCH_3$), ν_{max} (film) 1 740, 1 440, 1 280, 1 190, and 1 170 cm^{-1} , λ_{max} (cyclohexane) 200 (log ϵ 3.78) and 238 nm (3.98) [lit.⁹ for *O*-ethyl thioacetate, λ_{max} (cyclohexane) 241 (log ϵ 3.92)].

Reaction of 2,5-Dimethoxythiophen with Maleic Anhydride.

⁴ J. M. Barker, P. R. Huddleston, and M. L. Wood, *Synth. Comm.*, 1975, **5**, 59.

⁵ W. Steinkopf and M. Bauermeister, *Annalen*, 1914, **402**, 69.

⁶ D. J. Chadwick, J. Chambers, G. D. Meakins, and R. L. Snowden, *J.C.S. Perkin I*, 1973, 1766.

⁷ D. B. Clapp, *J. Amer. Chem. Soc.*, 1939, **61**, 2733.

⁸ R. Helder and H. Wynberg, *Tetrahedron Letters*, 1972, 605.

CH_3O), ν_{max} (KBr) 1 865, 1 790, 1 215, 1 085, 935 (five-membered cyclic anhydride^{10a}), and 1 620 cm^{-1} (bicyclo-[2.2.2]octene C=C^{10b}), λ_{max} (MeOH) 209 (log ϵ 3.09) and 238 nm (log ϵ 2.72) [a simple molecular model of (2) showed that the π -orbitals of one anhydride group are very close to those of the other, and this may account for the much stronger u.v. absorption than is normally observed for anhydrides],¹¹ m/e 210 (96%, loss of maleic anhydride¹²), 208 (28%, M - maleic anhydride - H_2), 138 (100%, 210 - CO - CO $_2$), and 123 (83%, 138 - CH_3).

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⁹ M. J. Janssen, *Rec. Trav. chim.*, 1960, **79**, 464.

¹⁰ IRSCOT-SYSTEM, Heyden and Son Ltd., London, 1963, (a) Table 4, card L1c; (b) Table 1, card K1.

¹¹ H. Ley and B. Arends, *Z. phys. Chem. (Leipzig)*, 1932, **B15**, 311; 1932, **B17**, 177.

¹² H. Budzikiewicz, J. I. Brauman, and C. Djerassi, *Tetrahedron*, 1965, **21**, 1855.